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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/616,228

07/08/2003

Mark S. Chee

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07/06/2007

AFFYMETRIX, INC

ATTN: CHIEF IP COUNSEL, LEGAL DEPT.

3420 CENTRAL EXPRESSWAY

SANTA CLARA, CA 95051

EXAMINER

WHALEY, PABLO S

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

07/06/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/616,228

Applicant(s)

CHEE ET AL.

Examiner

Pablo Whaley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-39 and 41-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-39 and 41-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6/5/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicants' remarks, filed 10/16/2006, have been fully considered. The following rejections and/or objections are maintained, newly applied, or withdrawn for the reasons set forth below. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 36-39 and 41-44.

Claims 1-35, 40, and 45 have been canceled.

PRIORITY

Priority to US Provisional Application 08/327,525, filed Oct. 21, 1994 has been acknowledged.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement filed 6/5/2006 has been considered in part. The "Illumina Inc." reference was not considered as not publication date or related page numbers were provide.

NEW MATTER

The amendment filed 08/09/2004 was objected to under 35 U.S.C. 132(a) for introducing priority documents into the specification, as added in the Transmittal letter filed 7/8/2003.

Applicant's arguments filed 10/16/2006 are persuasive. This rejection is hereby withdrawn.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 36-39 and 41-44 were rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter.

Applicant's arguments filed 10/16/2006 that "no concrete, tangible, and useful result" is required to be recited in the claims are not persuasive for the following reasons.

According to the revised Guidelines, a claimed invention directed to a statutory process must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))]. The revised Guidelines also state that the focus is "not on whether the steps taken to achieve a particular result are useful, tangible, and concrete, but rather on whether the final result achieved by the claimed invention is useful, tangible, and concrete." For an updated discussion of statutory considerations, see the revised Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV (Latest Revision August 2006).

Claims 36-39 are directed to method for identifying a mutation in a sample nucleic acid sequence. The Examiner maintains that claims 36-39, which are currently amended and now result in "identifying a mutation in a sample according to at least a ratio and pattern in the library," do not recite a physical transformation of matter (i.e. assay) and do not recite a tangible result, as this step can reasonably occur within a computer system. Therefore this rejection is

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maintained. This rejection could be overcome by amending the claims to recite a step wherein the intended result is "displayed" or "outputted" (e.g. output to a user, a display, a memory, or another computer, etc.), or by amending the claims to include a step of a physical transformation of matter (e.g. assay).

Claims 41-44 are now directed to computer program product stored in a computer readable medium for identifying a mutation in a sample nucleic acid sequence, as in claims 36-39, comprising computer code. The Examiner maintains that claims 41-44, which are currently amended and now recite a "computer code identifying a mutation in a sample according to at least a ratio and pattern in the library," do not recite a physical transformation of matter (i.e. assay). The Examiner also maintains that the recitation of "computer code that identifies a mutation" is not a tangible result, as this step can reasonably occur within a computer system such that a user of the claimed program would not know what the output of the claimed program actually consists of. For the above reasons, the instant claims lack a "tangible" result and thus do not recite more than a 35 U.S.C. 101 judicial exception. Therefore, this rejection is maintained. This rejection could be overcome by amending the claims to recite a computer readable medium comprising a program containing instructions, wherein the program result is "displayed" or "outputted" (e.g. output to a user, a display, a memory, or another computer, etc.), or by amending the claims to include a step of a physical transformation of matter (e.g. assay).

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 39, 42, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following rejections are maintained or necessitated by amendment.

Claims 37 and 42 recite the limitation "shape of the patterns". Applicant's arguments do not clarify the issue. The Examiner maintains that it remains unclear as to the metes and bounds of a "shape" of patterns. Clarification is again requested.

Claims 37 and 42 recite the limitation "destabilization". Applicant's arguments do not clarify the issue. The Examiner maintains that it remains unclear in what way the shape of the patterns in the library vary "according to the destabilization" as it relates to base positions. Clarification is again requested.

Claims 39 and 44 now recite the limitations "wherein probes corresponding to the probe intensities have a length and an interrogation position; the base position of the mutation...is identified utilizing the length of the probes and the interrogation position". Applicant's amendments do not clarify the issue. It remains unclear in what way "probes corresponding to the probe intensities have a length and an interrogation position" further limits the method of Claim 36. Clarification is again requested.

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 36-39 and 41-44 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying mutations by comparison of patterns of samples with "known" mutations does not reasonably provide enablement for identifying mutations by comparison to patterns of random samples.

Applicant's arguments, filed 10/16/2006, that sufficient guidance was provided in the specification are persuasive. This rejection is hereby withdrawn.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36-39 and 41-44 were rejected under 35 U.S.C. 102(e) as being anticipated by Webster et al. (US 6,600,996; Priority: Oct. 21, 1994)

Applicant's arguments, filed 10/16/2006, regarding priority of the Webster et al. reference are persuasive. This rejection is hereby withdrawn.

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Claims 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Wurst et al. (Proc. Natl. Acad. Sci, November 1991, Vol. 88, pp. 9909-9913). *This rejection is necessitated by amendment.*

Wurst et al. teach a method for identifying mutations in nucleic acid sequences [Abstract]. More specifically, Wurst et al. provide a selected library comprising hybridized DNA fragments with point specific mismatches in a mutagenesis window, and un-selected library comprising hybridized DNA fragments with all possible combinations of sequence mismatches in a mutagenesis window [p.9911, Col. 2, ¶ 2], as in claim 36; comparison of band intensities between selected and un-selected libraries, wherein increased band intensity is indicative of mutations [p.9911, Col. 2, ¶ 2, and Fig. 2]. As mutations are determined based on positions of bands between libraries as well as band intensities, and as the instant claims do not recite any step directed to calculation of a 'ratio' or limitations as to what said 'ratio' actually consists of, the Examiner has broadly interpreted this as a teaching for comparing patterns according to "ratios", as in claim 36. Wurst et al. also provide a statistical analysis of [p.9912, Col. 2] and summary of mutations detected [Fig. 4], as in claim 36; and analysis that includes a comparison to wild-type band intensities [p.9912, Col. 1, ¶ 2 and 3, and Fig. 3], as in claim 38. Wurst et al. also provide a comparison of 'shapes of patterns' in libraries that vary according to other detectable effects around the mutagenesis window (i.e. frameshift mutations) [p.9912, Col. 1, ¶ 5] and [Fig. 3, Lower], which the Examiner has broadly interpreted as a library varying according to 'destabilization' as in claims 37.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36-39 and 41-44 are rejected under 35 U.S.C. 103(a) as being made obvious by Staden et al. (Nucleic Acids Research, 1982, Vol. 10, No. 15, p. 4731-4751), in view of Rossiter et al. (The Journal of Biological Chemistry, 1990, Vol. 265, No. 22, p. 12753-12756). *This rejection is necessitated by amendment.*

Staden teaches a computer implemented method and a computer program product for the manipulation and storage of DNA sequencing data produced by the shotgun method. More specifically, Staden provides the following: a program compares a sample sequence obtained from calling bases from a sequencing gel reading ("gel readings", 2. SCREENV, p4737) to reference sequences ("vector sequence", p. 4737) and displays alignment of sample and reference, as in claims 36 and 41; a program that compares a batch of sequences with the consensus for a database (p.4738, ¶ 2), as in claims 36 and 41; an alignment method that returns information about the number of contigs a samples overlaps with and the positions of

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the matches (p.4743, ¶ 2-4); a program ("SCAN", p.4740, Section 11) that assigns values to sequence data for each base position and compares these values to user-defined percentages (i.e. ratio) to classify each base position, which the Examiner has broadly interpreted as a teaching for "ratios." The program displays difference between the reference, sample and user selected sequences (i.e. interrogation positions) (Figure 3, p. 4749), as in claims Staden teaches the storage of the computer readable program product ("in constant use", p.4748 and "written in fortran", p. 4751), as in claim 41.

Staden does not specifically recite 'a mutation in a nucleic acid sample', as in claims 36 and 41, or limitations directed to wild-type and destabilization, as in claims 37, 38, 42, and 43. However, Staden clearly teaches methods for determining mismatches in sequence data, as set forth above, which a minimum suggests applications for shotgun sequencing of mutation detection.

Rossiter et al. teach a plurality of methods for molecular scanning methods of mutation detection in nucleic acid sequences [Abstract]. More specifically, Rossiter et al. teach detection methods utilizing wild-type and mutant DNA sequences and labeled probes [Fig. 2 and 3], as in claims 36, 38, 41, and 42. In one particular method, points of mismatch (i.e. mutations) are depicted as a "bulge" [Fig. 3], which the Examiner has broadly interpreted as shape varying according to a 'destabilization', as in claims 37 and 42.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the automated shotgun sequencing method of Standen with the scanning mutation detection method and mutation data sets taught by Rossiter et al., as it is well known in the art that mutation detection is improved by coupling of scanning and sequence-based methods [Rossiter et al., p.12756, Col. 1, ¶ 2]. One of ordinary skill in the art would have been motivated to combine the above teachings to improve mutation detection using automation

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[Rossiter et al., p.12755, Col. 2, ¶ 7], resulting in the practice of the instant claimed invention. One of skill in the art would have had a reasonable expectation of successfully combining the above teachings as both Staden and Rossiter et al. teach methods for sequencing nucleic acid data.

Claims 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wurst et al. (Proc. Natl. Acad. Sci, November 1991, Vol. 88, pp. 9909-9913), as applied to claims 36-39 above, in view of the legal decision of *In re Venner* [262 F.2d91, 95, 120 USPQ 193, 194 (CCPA 1958)]. *This rejection is necessitated by amendment.*

Wurst et al. teach a method for identifying mutations in nucleic acid sequences [Abstract]. More specifically, Wurst et al. provide a selected library comprising hybridized DNA fragments with point specific mismatches in a mutagenesis window, and un-selected library comprising hybridized DNA fragments with all possible combinations of sequence mismatches in a mutagenesis window [p.9911, Col. 2, ¶ 2], as in claims 36 and 41; comparison of band intensities between selected and un-selected libraries, wherein increased band intensity is indicative of mutations [p.9911, Col. 2, ¶ 2, and Fig. 2]. As mutations are determined based on positions of bands between libraries as well as band intensities, and as the instant claims do not recite any step directed to calculation of a 'ratio' or limitations as to what said 'ratio' actually consists of, the Examiner has broadly interpreted this as a teaching for comparing patterns according to "ratios", as in claims 36 and 41. Wurst et al. also provide a statistical analysis of [p.9912, Col. 2] and summary of mutations detected [Fig. 4], as in claims 36 and 41, and analysis that includes a comparison to wild-type band intensities [p.9912, Col. 1, ¶ 2 and 3, and Fig. 3], as in claims 38 and 43. Wurst et al. also provide a comparison of 'shapes of patterns' in

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libraries that vary according to other detectable effects around the mutagenesis window (i.e. frameshift mutations) [p.9912, Col. 1, ¶ 5] and [Fig. 3, Lower], which the Examiner has broadly interpreted as a library varying according to 'destabilization' as in claims 37 and 42.

Wurst et al. do not specifically teach a computer program product and related code, as in claims 41-44.

In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.).

In re Venner is a legal decision which indicates that automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish the prior art in terms of patentability. Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to perform any step of the previously stated methods of Wurst et al. according to *In re Venner*.

CONCLUSION

No claims are allowed.

Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley
Patent Examiner
Art Unit 1631
Office: 571-272-4425
Direct Fax: 571-273-4425

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

